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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,851	09/19/2003	Peter Bodine	00630/100M091-US2	6790

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DARBY & DARBY P.C.
P.O. BOX 5257
NEW YORK, NY 10150-5257

EXAMINER	
XIE, XIAOZHEN	
ART UNIT	**PAPER NUMBER**
1646	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/666,851	BODINE, PETER	
	Examiner	Art Unit	
	Xiaozhen Xie	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-4 and 6-43* is/are pending in the application.

4a) Of the above claim(s) *7-19 and 26-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6 and 20-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 February 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 10/169,545.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Applicant's amendments of the specification and the claims received on 19 September 2006 have been entered.

Claim 5 has been cancelled. Claims 1-4 and 6-43 are pending. Claims 7-19 and 26-43 are withdrawn from further consideration as being drawn to a nonelected invention. Claims 1-4, 6 and 20-25 are under examination.

Specification

The objection of the specification for informalities is withdrawn in response to Applicant's amendment of the specification.

Claim Objections/Rejections Withdrawn

The objection of claim 1 for reciting non-elected species is withdrawn in response to Applicant's amendment of the claim.

The rejection of claims 1-6 and 20-24 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement, is withdrawn in response to Applicant's amendment of the claims to recite "sFRP-1 protein of SEQ ID NO: 2".

The rejection of claim 2 under 35 U.S.C. 103(a), as being unpatentable over Umansky, in view of Hoang, is withdrawn in response to Applicant's amendment of the claims to recite "sFRP-1 protein of SEQ ID NO: 2".

Claim Rejections Maintained/New Grounds of Rejections

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The amended claims 20-24 remain rejected under 35 U.S.C. § 112, first paragraph, as being lack of full enablement.

Applicant argues that the amendment of the claims, now reciting "an antibody against a secreted frizzled related protein-1 (sFRP-1) of SEQ ID NO: 2", has obviated the rejection. Applicant argues that the specification describes a number of desirable fragments of SEQ ID NO: 2, which could be used to generate antibodies for regulating bone-forming activity. Applicant argues that generating an antibody against a protein or protein fragment is routine for one skilled in the art.

Applicants' argument has been fully considered but has not been found to be persuasive.

The amendment of the claims is not sufficient to overcome the rejection, because the claims still read on a genus of antibodies that bind to sFRP-1 and fragments thereof, e.g., antibodies directed to a regulating portion of sFRP-1 of SEQ ID NO: 2, or antibodies raised against at least 8 or 10 consecutive amino acids of sFRP-1 of SEQ ID NO: 2, or antibodies raised against at least amino acids 217-231 of sFRP-1 of SEQ ID NO: 2. As stated previously, the specification discloses an antibody that specifically binds to sFRP-1 of SEQ ID NO: 2, encoded by a polynucleotide of SEQ ID NO: 1. The specification discloses that overexpression of sFRP-1 accelerates human osteoblast cell death (Example 12), and that an anti-peptide antisera generated to amino acids 217-231 of sFRP-1 inhibited cell death mediated by overexpression of this gene, e.g., 50-60 % of the cells alive after 3 days treatment with the antisera compared to 20-30%

of the cells alive in the control group. (Example 14 and Figure 12). The specification, however, has not provided sufficient teachings that antibodies directed to other fragments of sFRP-1 have the same binding and inhibiting specificity. On paragraph 106 of the published application, Applicant recites "In preferred embodiments, the antibody is raised against a sequence comprising amino acids 217-231 of a sFRP-1 protein, a polypeptide have the amino acid sequence set forth in SEQ ID NO: 2, or sequence variations thereof". As discussed previously, Specht et al. (DE19813835-A1) teach a human breast tumor-associated protein 38, which comprises the amino acids 217-231 of SEQ ID NO: 2 of the instant application, and antibody raised against this polypeptide would not be able to block sFRP-1, nor to promote bone-forming activity. The scope of patent protection sought by Applicant as defined by the claims fails to correlate reasonably with the scope of enabling disclosure set forth in the specification. Therefore, without undue experimentation, one skilled in the art would not know how to practice the invention as broadly claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 3, 4, 6, 20-25 are rejected under 35 U.S.C. 102(e) as being anticipated by Umansky et al. (U. S. Patent No: 6,433,155B1).

Applicant argues that claims 1 and 20 have been amended to recite "sFRP-1 protein of SEQ ID NO: 2", and the SARP proteins described by Umansky are not identical to the sFRP-1 protein of SEQ ID NO: 2. Applicant argues that Umansky does not teach a pharmaceutical composition for regulating bone-forming activity in a mammal, and thus fails to anticipate the instant application.

Applicants' argument has been fully considered but has not been found to be persuasive.

As set forth in the previous office action, Umansky teaches a pharmaceutical composition comprising an antibody against a polypeptide of the SARP (Secreted Apoptosis-Related Protein) family. SARP-2, also known as sFRP-1, shares a 99.7% similarity to the sFRP-1 protein of SEQ ID NO: 2 of the instant application, and has 100% identity in the amino acid sequence of residues 217-231 (sequence alignment provided in the previous office action). Umansky also teaches the encoding polynucleotide sequence, which has 98% local similarity to the instant SEQ ID NO: 1 (between nucleotide 6-1136) (see attached sequence alignment). Thus, even though the antigen of the prior art is not 100% identical to SEQ ID NO: 2 of the claims, one of ordinary skill in the art would reasonably expect that a substantial population of the antibodies encompassed by the prior art would bind against SEQ ID NO: 2, or the sFRP-1 protein obtained by the expression of the polynucleotide sequence of SEQ ID NO: 1. Umansky further teaches the pharmaceutically acceptable composition comprising the SARP antibody for treating patients suffering from a condition related to

apoptosis. Even though Umansky does not expressly teach that the pharmaceutical composition is for regulating bone-forming activity, this function would reasonably be considered to be inherent to the composition since it has exactly the same components recited in the claims. In addition, for the purpose of applying art, the preamble "for regulating bone-forming activity" is not given weight, since the composition is the same.

Claims 1, 3, 4, 6, 20-25 are newly rejected under 35 U.S.C. 102(e) as being anticipated by Rubin et al. (U. S. Patent No: 6,479,255B1, which has a provisional filing date on 29 May 1997).

Rubin teaches a polypeptide capable of specifically binding a FRP polypeptide, such as an antibody specific for a FRP polypeptide (column 4, lines 39-43, column 8, lines 18-28). Rubin teaches a pharmaceutical composition thereof comprising a pharmaceutically acceptable carrier (column 10, line 6-13). Rubin teaches the amino acid sequence of the FRP which has 95.5% similarity (96.5% local similarity) to SEQ ID NO: 2 of the instant application, and the polynucleotide sequence encoding the FRP which has a 97.4% similarity (99.0% local similarity) to SEQ ID NO: 1 of the instant application (see sequence alignments). Even though the polypeptide of the prior art is not 100% identical to the polypeptide of SEQ ID NO: 2 of the instant claims, one of ordinary skill in the art would reasonably expect that a substantial population of the antibodies encompassed by the prior art would bind against the polypeptide of SEQ ID NO: 2, or encoded by SEQ ID NO: 1. While Rubin does not expressly teach that the pharmaceutical composition is for regulating bone-forming activity in a mammal, this function would reasonably be considered to be inherent to the composition since it has

exactly the same components recited in the claims. A compound and all of its properties are inseparable (*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963)).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 2 is newly rejected under 35 U.S.C. 103(a) as being unpatentable over Umansky, in view of Warman et al. (WO 02/16553 A2, international publication date 28 February 2002).

Umansky teaches as set forth above, a pharmaceutical composition comprising an antibody against a polypeptide of SARP-2, also known as sFRP-1.

Umansky, however, does not teach that the sFRP-1 is from human osteoblast cells (claim 2).

WO 02/16553 teaches sFRP-1 expression in purified trabecular bone primary cells, NHBC (human bone-derived cells). WO 02/16553 teaches sFRP-1 expression in different fractions of the primary cells which contain osteoblasts corresponding to different differentiation state (pp. 69, Example 8, and Figure 8).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Umansky, with those of WO 02/16553 to prepare a pharmaceutical composition comprising an antibody against SARP-2 (sFRP-1), wherein the sFRP-1 protein is from human osteoblast cells. One of

ordinary skill in the art would have been motivated to make such antibody for the purpose of detecting the sFRP-1 protein in osteoblast cells. Therefore, the combined teachings provide a reasonable expectation of successfully preparing the composition.

Conclusion

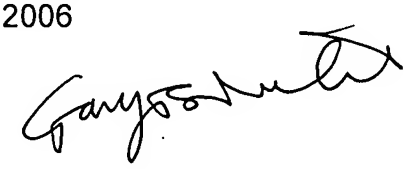
NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol, Ph.D. can be reached 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Xiaozhen Xie, Ph.D.
December 6, 2006



GARY B. NICKOL, PH.D.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600